5,908,697 which has been cited in the present Office action. Regardless of the specific composition disclosed by De Haan et al, the liposomes used by De Haan et al have a different structure from the vesicles according to the invention *which are not conventional liposomes* and withdrawal of this rejection is requested.

Claims 16-17 and 21-35 have been rejected under 35 USC 103(a) over De Haan et al alone or in combination with Roux et al.

As noted above, Roux et al does disclose the vesicles of the invention, but does not disclose or suggest using such vesicles as carriers for antigens. Since De Haan et al and Roux et al both involve liposomal structures, the question is then whether one could expect to substitute the structures of Roux et al for the conventional liposomes of De Haan et al and expect to achieve the same or improved results.

Applicants argue that the results are not the same, because the mechanism of action of De Haan et al is entirely different from that of the invention.

The first point to be made is that on page 159 of De Haan et al, in the second column, De Haan states quite clearly that the liposomes used must be negatively charged. De Haan et al states that with zwitterionic liposomes, consisting of PC and cholesterol alone, stimulation of antibody responses was not observed. De Haan et al speculates on page 161 that this could result from an increased uptake by macrophages of negatively charged liposomes.

To the contrary, the claimed invention does not require negatively charged liposomes and in fact, the examples show benefit from the administration of vesicles prepared with zwitterionic lipids, which do not function in the environment of De Haan et al. De Haan et al clearly teaches against the use of such materials.

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DENNISON, SCHULTZ, DOUGHERTY & MACDONALD
SUITE 105
1727 KING STREET
ALEXANDRIA, VIRGINIA 22314-2700
703 837-0550

Moreover, as disclosed in the second column on page 160, the De Haan et al disclosure involves a mechanism in which liposomes can be administered separately from the antigen and possess an immunoadjuvant activity unrelated to their potential role as an antigen-carrier system. For this reason, De Haan et al utilizes a large excess of liposomes, a ratio not lower than 500:1.

The results obtained in the present application have been obtained with a lipid to antigen weight ratio as low as 100:1, therefore at least five times less than the minimum ratio used by De Haan et al. In this case, the minimum ratio needed by De Haan et al is not linked to the specific antigen, but to the mechanism of action of the liposomes. The invention uses a contrary mechanism, one in which the antigen is incorporated in the vesicles, and with a much lower amount of lipid required.

Thus, one of ordinary skill in the art would not have expected the invention to function in the manner shown, the use of the vesicles of the invention producing a new mechanism of action. Withdrawal of this rejection is accordingly requested.

Claims 18-19 and 36-65 have been rejected under 35 USC 103(a) over De Haan et al by itself or in combination with Roux et al, and in further combination with Doerschuk. The Doerschuk reference has been cited show conventional techniques of purifying immunoglobuins, but does not otherwise cure the defects of the De Haan et al and Roux et al references, and withdrawal of this rejection is requested.

Claims 16 through 19, 21 through 33 and 35 through 65 have been rejected under 35 USC 103(a) over Wassaf et al in combination with De Haan et al by itself or in combination with Doerschuk and Roux et al.

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SUITE 105
1727 KING STREET
ALEXANDRIA, VIRGINIA 22314-2700
703 837-9600

Wassef et al has been cited for a showing of the use of liposomes as carriers for a vaccine, but does not disclose or suggest mucosal administration. The liposomes used are conventional liposomes, similar to De Haan et al, but not limited to negatively charged liposomes. Thus, for one of ordinary skill in the art having knowledge of these two references, the De Haan et al reference would be the proper reference to consider in terms of mucosal administration, and would have not reason to look to the Wassef et al reference which is not concerned with mucosal administration. Wassef et al therefore adds nothing to the rejection, being concerned with a different route for administration, and with a different mechanism of action, since Wassef is not limited to negatively charged liposomes. Withdrawal of this rejection is accordingly requested.

In view of the foregoing remarks, Applicants submit that the present application is now in condition for allowance, and an early allowance of the application is earnestly solicited.

Respectfully submitted,

Ira J. Schultz
Registration No. 28666

LAW OFFICES
DENNISON, SCHULTZ, DOUGHERTY & MACDONALD
SUITE 105
1727 KING STREET
ALEXANDRIA, VIRGINIA 22314-2700
703 837-9600